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FILE 'HOME' ENTERED AT 08:02:47 ON 03 FEB 2005

=> fil reg
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

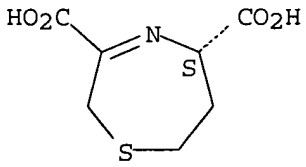
FILE 'REGISTRY' ENTERED AT 08:03:05 ON 03 FEB 2005

=> s cystathionine ketimine/cn
L1 1 CYSTATHIONINE KETIMINE/CN

=> d

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2005 ACS on STN
RN 87458-28-4 REGISTRY
CN 1,4-Thiazepine-3,5-dicarboxylic acid, 2,5,6,7-tetrahydro-, (5S)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1,4-Thiazepine-3,5-dicarboxylic acid, 2,5,6,7-tetrahydro-, (S)-
OTHER NAMES:
CN **Cystathionine ketimine**
FS STEREOSEARCH
MF C7 H9 N O4 S
CI COM
LC STN Files: BIOSIS, CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

23 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
23 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> fil .bec
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	7.30	7.51

FILES 'MEDLINE, SCISEARCH, LIFESCI, BIOTECHDS, BIOSIS, EMBASE, HCAPLUS, NTIS, ESBIOBASE, BIOTECHNO, WPIDS' ENTERED AT 08:04:31 ON 03 FEB 2005

11 FILES IN THE FILE LIST

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FILE 'MEDLINE'
L2            0 L1

FILE 'SCISEARCH'
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L3            0 CYSTATHIONINE KETIMINE/CN

FILE 'LIFESCI'
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L4            0 CYSTATHIONINE KETIMINE/CN

FILE 'BIOTECHDS'
L5            0 CYSTATHIONINE KETIMINE/CN

FILE 'BIOSIS'
L6           11 L1

FILE 'EMBASE'
L7            0 L1

FILE 'HCAPLUS'
L8           23 L1

FILE 'NTIS'
'CN' IS NOT A VALID FIELD CODE
L9            0 CYSTATHIONINE KETIMINE/CN

FILE 'ESBIOBASE'
'CN' IS NOT A VALID FIELD CODE
L10           0 CYSTATHIONINE KETIMINE/CN

FILE 'BIOTECHNO'
L11           0 L1

FILE 'WPIDS'
L12           0 CYSTATHIONINE KETIMINE/CN

TOTAL FOR ALL FILES
L13          34 L1

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PROCESSING COMPLETED FOR L13
L14           23 DUP REM L13 (11 DUPLICATES REMOVED)

=> d tot

L14  ANSWER 1 OF 23  HCAPLUS  COPYRIGHT 2005 ACS on STN
TI   Antagonists of D-amino acid oxidase and D-aspartate oxidase for treatment
     of central nervous sytem disorders
SO   U.S. Pat. Appl. Publ., 138 pp., Cont.-in-part of U.S. Ser. No. 51,681.
     CODEN: USXXCO
IN   Cohen, Daniel; Chumakov, Llya
AN   2003:696521  HCAPLUS
DN   139:224389
     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     --------------      ----   --------    --------------------   --------
PI   US 2003166554        A1    20030904    US 2002-211160         20020801
     US 2003185754        A1    20031002    US 2002-51681          20020116

L14  ANSWER 2 OF 23  HCAPLUS  COPYRIGHT 2005 ACS on STN
TI   Treatment of CNS disorders using D-amino acid oxidase and D-aspartate
     oxidase antagonists
SO   PCT Int. Appl., 194 pp.
```

CODEN: PIXXD2
IN Cohen, Daniel; Chumakov, Ilya
AN 2002:658287 HCAPLUS
DN 137:195529

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002066672	A2	20020829	WO 2002-IB1262	20020115
WO 2002066672	A3	20040226		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2433866	AA	20020829	CA 2002-2433866	20020115
EP 1412515	A2	20040428	EP 2002-717019	20020115
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004537275	T2	20041216	JP 2002-566376	20020115

L14 ANSWER 3 OF 23 HCAPLUS COPYRIGHT 2005 ACS on STN
TI Cystathionine metabolism in patients with cystathioninuria and effect of priming of cystathionine metabolites on superoxide generation in human neutrophils
SO Recent Research Developments in Biophysics & Biochemistry (2001), 1, 189-199
CODEN: RRDBDN
AU Kodama, Hiroyuki; Zhang, Jianying; Sugahara, Kazunori; Sagara, Yasuhiro; Masuoka, Yoshinori
AN 2002:623127 HCAPLUS
DN 138:13150

L14 ANSWER 4 OF 23 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN DUPLICATE 1
TI Accumulation of cystathionine, cystathionine ketimine, and perhydro-1,4-thiazepine-3,5-dicarboxylic acid in whole brain and various regions of the brain of D,L-propargylglycine-treated rats.
SO Metabolism Clinical and Experimental, (August, 2000) Vol. 49, No. 8, pp. 1025-1029. print.
CODEN: METAAJ. ISSN: 0026-0495.
AU Yu, Shirong; Sugahara, Kazunori; Nakayama, Kazuko; Awata, Shiro; Kodama, Hiroyuki [Reprint author]
AN 2000:397705 BIOSIS

L14 ANSWER 5 OF 23 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN DUPLICATE 2
TI Novel priming compounds of cystathionine metabolites on superoxide generation in human neutrophils.
SO Biochemical and Biophysical Research Communications, (March 16, 2000) Vol. 269, No. 2, pp. 297-301. print.
CODEN: BBRCA9. ISSN: 0006-291X.
AU Kodama, Hiroyuki [Reprint author]; Zhang, Jianying [Reprint author]; Sugahara, Kazunori [Reprint author]
AN 2000:166437 BIOSIS

L14 ANSWER 6 OF 23 HCAPLUS COPYRIGHT 2005 ACS on STN
TI d-Cystathionine Ketimine and l-Cystathionine Ketimine Enhance Superoxide Generation by Human Neutrophils in a Different Manner
SO Archives of Biochemistry and Biophysics (1999), 363(1), 55-59
CODEN: ABBIA4; ISSN: 0003-9861

AU Zhang, Jianying; Zhang, Meiying; Sugahara, Kazunori; Sagara, Yasuhiro; Spirito, Alessandra; Dupre, Silvestro; Kodama, Hiroyuki
AN 1999:134071 HCAPLUS
DN 130:334222

L14 ANSWER 7 OF 23 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN DUPLICATE 3
TI Metabolism of cystathionine, N-monoacetylcystathionine, perhydro-1,4-thiazepine-3,5-dicarboxylic acid, and cystathionine ketimine in the liver and kidney of D,L-propargylglycine-treated rats.
SO Metabolism Clinical and Experimental, (Oct., 1998) Vol. 47, No. 10, pp. 1233-1238. print.
CODEN: METAAJ. ISSN: 0026-0495.
AU Zhang, Jianying; Zhang, Meiying; Ma, Deshun; Sugahara, Kazunori; Kodama, Hiroyuki [Reprint author]
AN 1998:497876 BIOSIS

L14 ANSWER 8 OF 23 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN DUPLICATE 4
TI Detection of cystathionine ketimine and lanthionine ketimine in human brain.
SO Neurochemical Research, (1997) Vol. 22, No. 7, pp. 821-824.
CODEN: NEREDZ. ISSN: 0364-3190.
AU Fontana, Mario [Reprint author]; Brunori, Andrea; Costa, Mara; Antonucci, Antonio
AN 1997:355978 BIOSIS

L14 ANSWER 9 OF 23 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN DUPLICATE 5
TI Effect of cystathionine and cystathionine metabolites on the phosphorylation of tyrosine residues in human neutrophils.
SO Biochemical and Biophysical Research Communications, (1996) Vol. 224, No. 3, pp. 849-854.
CODEN: BBRCA9. ISSN: 0006-291X.
AU Zhang, Jianying; Sagara, Yasuhiro; Fontana, Mario; Dupre, Silvestro; Cavallini, Doriano; Kodama, Hiroyuki [Reprint author]
AN 1996:432372 BIOSIS

L14 ANSWER 10 OF 23 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN DUPLICATE 6
TI Effect of cystathionine ketimine on the stimulus coupled responses of neutrophils and their modulation by various protein kinase inhibitors.
SO Biochemical and Biophysical Research Communications, (1996) Vol. 218, No. 1, pp. 371-376.
CODEN: BBRCA9. ISSN: 0006-291X.
AU Zhang, Jianying; Sugahara, Kazunori; Sagara, Yasuhiro; Fontana, Mario; Dupre, Silvestro; Kodama, Hiroyuki [Reprint author]
AN 1996:107963 BIOSIS

L14 ANSWER 11 OF 23 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN DUPLICATE 7
TI Identification of perhydro-1,4-thiazepine-3,5-dicarboxylic acid, cystathionine mono-oxo acids, cystathionine ketimines, cystathionine sulfoxide and N-acetylcystathionine sulfoxide in the urine sample of D,L-propargylgylycine treated rats.
SO Physiological Chemistry and Physics and Medical NMR, (1995) Vol. 27, No. 3, pp. 203-216.
CODEN: PCPNER. ISSN: 0748-6642.
AU Machida, Yumiko; Zhang, Jianying; Hashimoto, Kazuko; Wakiguchi, Hiroshi; Karashige, Takanobu; Masuoka, Noriyoshi; Ubuka, Toshihiko; Kodama, Hiroyuki [Reprint author]
AN 1996:221747 BIOSIS

L14 ANSWER 12 OF 23 HCAPLUS COPYRIGHT 2005 ACS on STN

TI Characterization of [35S]lanthionine ketimine specific binding to bovine brain membranes
SO Biochemical and Biophysical Research Communications (1993), 195(2), 673-8
CODEN: BBRCA9; ISSN: 0006-291X
AU Dupre, S.; Fontana, M.; Costa, M.; Pecci, L.; Ricci, G.; Cavallini, D.
AN 1993:664740 HCAPLUS
DN 119:264740

L14 ANSWER 13 OF 23 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN DUPLICATE 8
TI Reversible cyclization of S-(2-oxo-2-carboxyethyl)-L-homocysteine to cystathionine ketimine.
SO Amino Acids (Vienna), (1993) Vol. 4, No. 1-2, pp. 133-140.
ISSN: 0939-4451.
AU Solinas, S. P.; Pecci, L.; Montefoschi, G.; Fontana, M.; Cavallini, D. [Reprint author]
AN 1993:294606 BIOSIS

L14 ANSWER 14 OF 23 HCAPLUS COPYRIGHT 2005 ACS on STN
TI The reducing activity of S-aminoethylcysteine ketimine and similar sulfur-containing ketimines
SO Biochemical and Biophysical Research Communications (1992), 183(2), 481-6
CODEN: BBRCA9; ISSN: 0006-291X
AU Solinas, S. P.; Pecci, L.; Montefoschi, G.; Cavallini, D.
AN 1992:190589 HCAPLUS
DN 116:190589

L14 ANSWER 15 OF 23 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN DUPLICATE 9
TI DETECTION OF CYSTATHIONINE KETIMINE IN BOVINE CEREBELLUM.
SO Journal of Neurochemistry, (1990) Vol. 55, No. 5, pp. 1599-1602.
CODEN: JONRA9. ISSN: 0022-3042.
AU RICCI G [Reprint author]; VESCI L; MATARESE R M; ANTONUCCI A; MAGGIO A; PECCI L; CAVALLINI D
AN 1991:7553 BIOSIS

L14 ANSWER 16 OF 23 HCAPLUS COPYRIGHT 2005 ACS on STN
TI [35S]Lanthionine ketimine binding to bovine brain membranes
SO Biochemical and Biophysical Research Communications (1990), 171(1), 480-6
CODEN: BBRCA9; ISSN: 0006-291X
AU Fontana, M.; Ricci, G.; Solinas, S. P.; Antonucci, A.; Serao, I.; Dupre, S.; Cavallini, D.
AN 1990:608702 HCAPLUS
DN 113:208702

L14 ANSWER 17 OF 23 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN DUPLICATE 10
TI INFLUENCE OF DIET ON CYSTATHIONINE KETIMINE AND LANTHIONINE KETIMINE CONTENT IN HUMAN URINE.
SO Italian Journal of Biochemistry (English Edition), (1990) Vol. 39, No. 2, pp. 100-105.
CODEN: IJBIAC. ISSN: 0021-2938.
AU ANTONUCCI A [Reprint author]; PECCI L; FONTANA M; CAVALLINI D
AN 1990:379809 BIOSIS

L14 ANSWER 18 OF 23 HCAPLUS COPYRIGHT 2005 ACS on STN
TI Detection of cystathionine and lanthionine ketimines in human urine
SO Biochemistry International (1988), 17(5), 877-83
CODEN: BIINDF; ISSN: 0158-5231
AU Pecci, L.; Antonucci, A.; Nardini, M.; Cavallini, D.
AN 1989:91483 HCAPLUS
DN 110:91483

L14 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2005 ACS on STN

TI Bovine brain ketimine reductase
SO Biochimica et Biophysica Acta (1988), 957(2), 286-92
CODEN: BBACAQ; ISSN: 0006-3002
AU Nardini, M.; Ricci, G.; Vesci, L.; Pecci, L.; Cavallini, D.
AN 1989:35904 HCAPLUS
DN 110:35904

L14 ANSWER 20 OF 23 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN DUPLICATE 11
TI PROPERTIES OF THE PHENYLTHIOHYDANTOIN DERIVATIVES OF SOME SULFUR-CONTAINING CYCLIC AMINO ACIDS.
SO Physiological Chemistry and Physics and Medical NMR, (1988) Vol. 20, No. 3, pp. 199-204.
CODEN: PCPNER. ISSN: 0748-6642.
AU PECCI L [Reprint author]; COSTA M; PINNEN F; ANTONUCCI A; CAVALLINI D
AN 1989:199153 BIOSIS

L14 ANSWER 21 OF 23 HCAPLUS COPYRIGHT 2005 ACS on STN
TI The conversion of L-cystathionine into the cyclic ketimine form by heated rat liver extracts containing cystathionase and transaminase activities
SO Biochemistry International (1985), 10(4), 641-6
CODEN: BIINDF; ISSN: 0158-5231
AU Cavallini, D.; Costa, M.; Pensa, B.; Coccia, R.
AN 1985:218849 HCAPLUS
DN 102:218849

L14 ANSWER 22 OF 23 HCAPLUS COPYRIGHT 2005 ACS on STN
TI Ketimine formation by interacting L-cystathionine with glyoxylic acid
SO IRCS Medical Science (1984), 12(6), 468-9
CODEN: IMSCE2; ISSN: 0268-8220
AU Costa, Mara; Pensa, Bernardo; Cavallini, Doriano
AN 1984:565730 HCAPLUS
DN 101:165730

L14 ANSWER 23 OF 23 HCAPLUS COPYRIGHT 2005 ACS on STN
TI Similarity of the oxidation products of L-cystathionine by L-amino acid oxidase to those excreted by cystathioninuric patients
SO Journal of Biological Chemistry (1983), 258(17), 10511-17
CODEN: JBCHA3; ISSN: 0021-9258
AU Ricci, Giorgio; Santoro, Luigi; Achilli, Marco; Matarese, Rosa Marina; Nardini, Mirella; Cavallini, Doriano
AN 1983:573974 HCAPLUS
DN 99:173974

=> d ab 3-23

L14 ANSWER 3 OF 23 HCAPLUS COPYRIGHT 2005 ACS on STN
AB We have identified cystathionine metabolites, S-(3-hydroxy-3-carboxy-n-propyl)cysteine (HCPC), S-(2-carboxyethyl)cysteine(β-CEC), S-(carboxymethyl) homocysteine (CMHC), S-(2- hydroxy-2-carboxyethyl)homocysteine (HCEHC), N-monoacetylcystathionine, cystathionine sulfoxide, cystathionine ketimine (CK) and perhydro-1,4-thiazepine-3,5-dicarboxylic acid (PHTZDC) in the urine of cystathioninuric patient and the urine and several tissues of D,L-propargylglycine-treated rats. To clarify the physiol. function of cystathionine and cystathionine metabolites found in the urine of patients with cystathioninuria. Human peripheral blood polymorphonuclear leukocytes were preincubated with cystathionine and cystathionine metabolites. Among the cystathionine metabolites, cystathionine ketimine and cystathionine sulfoxide significantly enhanced the N-formylmethionylleucyl-phenylalanine (fMLP)- induced superoxide generation, but cystathionine, NAc-cystathionine and cyclothionine did not enhance the superoxide generation. The effects of D-cystathionine

ketimine (D-CK) and L-cystathionine ketimine (L-CK) on the stimulus-induced superoxide generation were compared. D-CK enhanced the superoxide generation induced by arachidonic acid (AA), phorbol 12-myristate 13-acetate (PMA) and fMLP showing a dependence on D-CK concentration

L-CK largely enhanced the fMLP-induced superoxide generation, whereas it showed no effect on these induced by AA and PMA. L-Cystathionine sulfoxides were separated into 2 diastereoisomers, CS-I and CS-II. CS-I enhanced the superoxide generation induced by AA and PMA, but not that induced by fMLP and opsonized zymosan (OZ). In contrast, CS-II enhanced the superoxide generation induced by fMLP and OZ, but not that induced by AA and PMA.

L14 ANSWER 4 OF 23 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN DUPLICATE 1

AB Experimental cystathioninuria was induced in rats by administration of the cystathionine gamma-lyase inhibitor, D,L-propargylglycine. The cystathionine metabolites, cystathionine ketimine (CK) and perhydro-1,4-thiazepine-3,5-dicarboxylic acid (PHTZDC), were identified in whole brain and various regions of the brain in D,L-propargylglycine-treated rats. The concentration of CK and PHTZDC in whole brain and various regions of the brain increased gradually after administration of D,L-propargylglycine, and reached the highest value at about 20 hours. CK and PHTZDC accumulated in whole brain and various regions of the brain in proportion to the amount of accumulated cystathionine after D,L-propargylglycine administration. The concentration of these compounds in the cerebellum was higher versus the other regions of the rat brain.

L14 ANSWER 5 OF 23 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN DUPLICATE 2

AB Human peripheral blood polymorphonuclear leukocytes were preincubated with cystathionine and cystathionine metabolites found in the urine of patients with cystathioninuria. Among the cystathionine metabolites, cystathionine ketimine and N-acetyl-S-(3-oxo-3-carboxy-n-propyl) cysteine (NAc-OCPC) significantly enhanced the N-formylmethionylleucylphenyl-alanine (fMLP)-induced superoxide generation, but cystathionine, NAc-cystathionine, and cyclothionine did not enhance the superoxide generation. Cystathionine ketimine and NAc-OCPC also enhanced superoxide generation induced by opsonized zymosan (OZ) but not that induced by arachidonic acid (AA) and phorbol 12-myristate 13-acetate (PMA). Superoxide generation induced by cystathionine ketimine and NAc-OCPC was inhibited by genistein, an inhibitor of tyrosine kinase, and was enhanced by 1-(5-isoquinoline sulfonyl)-2-methylpiperazine (H-7), an inhibitor of protein kinase C. Cystathionine ketimine and NAc-OCPC markedly also increased phosphorylation of 45-kDa protein in human neutrophils and the phosphorylation depended on the concentrations of cystathionine ketimine and NAc-OCPC. The phosphorylation of 45-kDa protein induced by cystathionine ketimine and NAc-OCPC was inhibited by genistein and herbimycin A, inhibitors of tyrosine kinase, but was not inhibited by H-7 and staurosporine, inhibitors of protein kinase C. Cystathionine metabolites and L-cystathionine sulfoxides were separated into two diastereoisomers, CS-I and CS-II. CS-I enhanced the superoxide generation induced by AA and PMA but not that induced by fMLP and OZ. In contrast, CS-II enhanced the superoxide generation induced by fMLP and OZ, but not that induced by AA and PMA.

L14 ANSWER 6 OF 23 HCAPLUS COPYRIGHT 2005 ACS on STN

AB The effects of d-cystathionine ketimine (D-CK) and l-cystathionine ketimine (L-CK) on the stimulus-induced superoxide generation by human neutrophils were compared. When the cells were preincubated with D-CK, the superoxide generation induced by arachidonic acid (AA), phorbol 12-myristate 13-acetate (PMA), and N-formyl-methionyl-leucyl-phenylalanine (fMLP) were enhanced, showing a dependence on D-CK concentration The rate of enhancement by D-CK was AA > PMA > fMLP. On the contrary, L-CK largely

enhanced the fMLP-induced superoxide generation, whereas it showed no effect on those induced by AA and PMA. The superoxide generations induced by AA and PMA in the D-CK-treated cells were suppressed by staurosporine, while those in the L-CK-treated cells were not affected. Genistein suppressed the fMLP-induced superoxide generation in the L-CK-treated cells more efficiently than that in the D-CK-treated cells. D-CK enhanced seryl phosphorylation of 16.5-kDa protein in human neutrophils, while L-CK enhanced tyrosyl phosphorylation of 45-kDa protein. (c) 1999 Academic Press.

L14 ANSWER 7 OF 23 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN DUPLICATE 3

AB Experimental cystathioninuria was induced by injection of D,L-propargylglycine in rats. The novel cystathionine metabolites, N-monoacetylcystathionine (NAc-cysta), perhydro-1,4-thiazepine-3,5-dicarboxylic acid (PHTZDC), and cystathionine ketimine (CK), were identified previously in the urine of patients with cystathioninuria and D,L-propargylglycine-treated rats. In this study, we identified these compounds in the liver and kidney of D,L-propargylglycine-treated rats using liquid chromatography-mass spectrometry with an atmospheric pressure chemical ionization interface system (LC/APCI-MS) and an amino acid analyzer. The metabolism of these compounds in the liver and kidney of D,L-propargylglycine-treated rats was also studied. PHTZDC, NAc-cysta, and CK were accumulated in the rat tissues in proportion to the content of cystathionine after D,L-propargylglycine administration. The concentrations of these compounds in the liver were higher than those in the kidney, and these compounds reached maxima earlier in the liver than in the kidney.

L14 ANSWER 8 OF 23 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN DUPLICATE 4

AB The sulfur containing imino acids cystathionine ketimine (CK) and lanthionine ketimine (LK) have been detected in the human brain by an HPLC procedure. The HPLC procedure takes advantage of the selective absorbance at 380 nm of the phenylisothiocyanate-ketimine adduct. Quantitation of cystathionine ketimine and lanthionine ketimine indicates a mean concentration (mean +- SD, n = 4) of 2.3 +- 0.8 nmol/g for CK and of 1.1 +- 0.3 nmol/g for LK in four human cerebral cortex samples of neurosurgical source. The identification of these cyclic ketimine derivatives of L-cystathionine and L-lanthionine as normal human metabolites in human nervous tissue may have interesting metabolic and physiological implications.

L14 ANSWER 9 OF 23 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN DUPLICATE 5

AB The effect of cystathionine and cystathionine metabolites found in the urine of patients with cystathioninuria on the phosphorylation of tyrosine residues was studied with human peripheral blood polymorphonuclear leukocytes. Among the cystathionine metabolites, cystathionine ketimine markedly increased phosphorylation of a 45 kDa protein with time and the phosphorylation depended on the concentration of cystathionine ketimine, while cystathionine and the reduced form of cystathionine ketimine (cyclothionine) did not increase the phosphorylation of the 45 kDa protein. The phosphorylation of the 45 kDa protein induced by cystathionine ketimine was inhibited by genistein and herbimycin A, inhibitors of tyrosine kinase, but was not inhibited by 1-(5-isoquinolinesulfonyl)-2-methylpiperazine and staurosporine, inhibitors of protein kinase C.

L14 ANSWER 10 OF 23 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN DUPLICATE 6

AB Human peripheral blood polymorphonuclear leukocytes were preincubated with cystathionine and cystathionine metabolites found in the urine of the patients with cystathioninuria. Among the cystathionine metabolites,

cystathionine ketimine significantly enhanced the N-formyl-methionyl-leucyl-phenylalanine-induced superoxide generation, but cystathionine and cyclothionine did not enhance the superoxide generation. Cystathionine ketimine also enhanced superoxide generation induced by opsonized zymosan but not those induced by arachidonic acid and phorbol myristate acetate. Superoxide generation induced by cystathionine ketimine was inhibited by genistein, an inhibitor of tyrosine kinase, and was enhanced by 1-(5-isoquinoline-sulfonyl)-2-methyl-piperazine, an inhibitor of protein kinase C.

L14 ANSWER 11 OF 23 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN DUPLICATE 7

AB Novel cystathionine metabolites, perhydro-1,4-thiazepine-3,5-dicarboxylic acid (PHTZDC), cystathionine mono-oxo acids (S-(3-oxo-3-carboxy-n-propyl)cysteine and S-(2-oxo-2-carboxyethyl)homocysteine), cystathionine ketimines, cystathionine sulfoxide and N-acetylcystathionine sulfoxide were identified previously in the urine of patients with cystathioninuria. We have identified these compounds for the first time in the urine of D,L-propargylglycine-treated rats using LC/APCl-MS (liquid chromatography-mass spectrometry with an atmospheric Pressure chemical ionization interface system) and an amino acid analyzer. Cystathionine mono-oxo acids and cystathionine ketimines were easily interconvertible depending on the pH of the solution. The excretion of PHTZDC, total cystathionine ketimine (cystathionine mono-oxo acids plus cystathionine ketimines), cystathionine sulfoxide and Nac- cystathionine sulfoxide in the rat urine increased in proportion to that of cystathionine content after D,L-propargylglycine administration.

L14 ANSWER 12 OF 23 HCAPLUS COPYRIGHT 2005 ACS on STN

AB [35S]Lanthionine ketimine binds specifically and with high affinity to bovine brain membranes. This binding has been studied in detail. It is reversible, not occurring at an uptake site or at a metabolizing enzyme and depending only weakly on ionic strength; it is affected by thiol reagents. [35S]Lanthionine ketimine specific binding is displaced only by other ketimines and by catecholamines, but not by more selective adrenergic ligands; binding parameters are reported. [3H]Adrenaline but not [3H]dihydroalprenolol is partially displaced by lanthionine ketimine. With bovine brain prepns. a significant stimulation of basal adenylate cyclase activity by lanthionine ketimine is observed

L14 ANSWER 13 OF 23 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN DUPLICATE 8

AB S-(2-oxo-2-carboxyethyl)homocysteine (OCEHC), produced by the enzymatic monodeamination of cystathionine, is known to cyclize producing the seven membered ring of cystathionine ketamine (CK) which has been recognized as a cystathionine metabolic in mammals. Studies have been undertaken in order to find the best conditions of cyclization of synthetic OCEHC to CK and for the preparation of solid CK salt product. It has been found that ring closure takes place at alkaline pH and is highly accelerated in 0.5 M phosphate buffer. The sodium salt of CK has been prepared by controlled additions of NaOH to water-ethanol solution of OCEHC under N-2 atmosphere. A solid product is obtained which, dissolved in water, shows the spectral features of CK. Solutions of the sodium salt of CK show the presence of a pH depending reversible equilibrium with the open OCEHC form. Plot of the absorbance at 296 nm in function of pH indicates that at pH 9 the compound is completely cyclized while at pH 6 is totally in the open OCEHC form. At intermediate pHs variable ratios between the two forms occur. According to the results obtained by the spectral analysis, HPLC assays of the sodium salt of CK show different patterns depending on the pH of the elution buffer.

L14 ANSWER 14 OF 23 HCAPLUS COPYRIGHT 2005 ACS on STN

AB S-Aminoethylcysteine ketimine and other S-containing similar ketimines reduce mol. O and phospho-18-tungstate (Folin Marenzi reagent), although the S

atom is formally present in the nonreducing thioether form. 2,6-Dichlorophenolindophenol, some ferrihemoproteins, and other reagents are also reduced by this group of ketimines. Ferricytochrome c is reduced faster than metHb, metmyoglobin, and free hematin, whereas horseradish peroxidase compound I is reduced at once. These results indicate a wider reducing activity of this type of ketimine. The oxidation of ketimines by ferric cytochrome c appears a relevant finding pointing to a new possible way of enzymic modification of S-ketimines in tissues.

L14 ANSWER 15 OF 23 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN DUPLICATE 9

AB A new sulfur-containing cyclix imino acid, cystathionine ketimine, has been detected in bovine cerebellum by gas chromatography, gas chromatography-mass spectrometry, and high pressure liquid chromatography procedures. Gas chromatography and gas-mass analyses are based on derivatization of endogenous cystathionine ketimine with diazomethane after a simple enrichment procedures. The high pressure liquid chromatography procedure takes advantage of the selective absorbance at 380 nm of the phenyl isothiocyanate-ketimine interaction product. The concentration of this new sulfur imino acid found in a pool of four bovine cerebella is .apprx. 0.5 nmol/g.

L14 ANSWER 16 OF 23 HCAPLUS COPYRIGHT 2005 ACS on STN

AB 2H-1,4-Thiazine-5,6-dihydro-3,5-dicarboxylic acid (trivial name: lanthionine ketimine) (I) is a cyclic S-containing imino acid detected in bovine brain exts. This compound has been synthesized in a heavily labeled form starting from L-[35S]cysteine and purified by HPLC. The existence of a saturable and reversible binding of [35S]lanthionine ketimine to bovine brain membranes was demonstrated. A single population of binding sites with a concentration of 260 fmol/mg protein and a dissociation constant of 58 nM is present. Specific binding is competitively inhibited by other structurally similar imino acids, namely S-aminoethyl-L-cysteine ketimine (II), and cystathionine ketimine (III). These results suggest a possible functional role for these ketimines in the nervous system.

L14 ANSWER 17 OF 23 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN DUPLICATE 10

AB A simple HPLC procedure for the routine analyses of Cystathionine ketimine (CK) and Lanthionine ketimine (LK) content in human urine has been developed. The values obtained in morning urine of fifteen healthy subjects (both sexes, 25-45 years old) on a common mixed diet are 330-2480 μg/g creatinine (mean 1110) of CK and 100-420 μg/g creatinine (mean 200) of LK. Quantitation of the two ketimines in urine of subjects on strictly vegetarian diet indicate that while the excretion of LK is independent of the diet, the excretion of CK is significantly decreased in conditions of vegetarian diet.

L14 ANSWER 18 OF 23 HCAPLUS COPYRIGHT 2005 ACS on STN

AB A recently developed HPLC procedure for the determination of cystathionine ketimine (CK) and lanthionine ketimine (LK) has been applied to the detection of these compds. in human urine. The assay has taken advantage of the selective production of an absorbance at 380 nm, not seen with other amino acids, when the two ketimines are reacted with phenylisothiocyanate. Coelution with authentic phenylthiohydantoin derivs. of CK and LK and the identical absorption spectra establish the identity of the compds. found in the urine with the synthetic products. Quantitation of the two ketimines by HPLC indicates that the excretion of CK and LK is resp. 606 μg and 84 μg per g of creatinine as mean values of healthy subjects of both sexes, 20-40 yr old, in the early morning voided urine.

L14 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2005 ACS on STN

AB An NAD(P)H-dependent reductase was purified from bovine brain. It actively reduces a new class of cyclic unsatd. compds., named ketimines.

Ketimines arise from the transamination of some S-containing amino acids, such as L-cystathionine, S-aminoethyl-L-cysteine and L-lanthionine. The enzyme also reduces Δ1-piperidine 2-carboxylate, the C analog of aminoethylcysteine ketimine. Some kinetic and mol. properties of this enzyme were determined Subcellular localization and regional brain distribution were also studied. The ketimine reductase activity was associated with the soluble fraction, and was located prevalently in the cerebellum and cerebral cortex. Cyclothionine and 1,4-thiomorpholine-3,5-dicarboxylic acid, the enzymic reduction products of cystathionine ketimine and lanthionine ketimine, resp., were detected in bovine brain, thus suggesting a role of this enzyme in their biosynthesis.

L14 ANSWER 20 OF 23 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN DUPLICATE 11

AB 1,4-thiomorpholine-3-carboxylic acid (TMA), hexahydro-1,4-thiazepine-3,5-dicarboxylic acid (cyclothionine) and their respective unsaturated analogues lanthionine ketimine (LK) and cystathionine ketimine (CK) react with phenylisothiocyanate to give the phenylthiohydantoin (PTH) derivatives without acidification and heating steps. Moreover the PTH-derivatives of the ketimines show a characteristic absorption maximum at 380 nm. Treatment with 1 M ammonia at 100° C converts the PTH-TMA in the corresponding PTH-ketimine. These properties are peculiar of these cyclic sulfur compounds.

L14 ANSWER 21 OF 23 HCAPLUS COPYRIGHT 2005 ACS on STN

AB Rat liver homogenates heated for 10 min at 60° and incubated with L-cystathionine yield cystathionine ketimine, which was identified by its typical UV spectrum and by co-chromatog. with authentic samples on the amino acid analyzer. Alanine and α-aminobutyric acid were also detected among the final products. The reaction is due to heat-stable γ-cystathionase and transaminases present in the exts. Cystathionase produces α-keto butyric acid and pyruvic acid, which are then used for the transamination of the remaining cystathionine to yield the ketimine. This is the 1st report indicating the occurrence in a mammalian tissue of an enzymic system using cystathionine for reactions differing from the traditional transulfuration to cysteine.

L14 ANSWER 22 OF 23 HCAPLUS COPYRIGHT 2005 ACS on STN

AB Cystathionine ketimine was formed from L-cystathionine by nonenzymic transamination with glyoxylic acid. The reaction was optimum at pH 10 and was stimulated by 50% in the presence of 10-4M CuCl2. This reaction is a possible alternative mechanism for the enzymic deamination and cyclization of cystathionine.

L14 ANSWER 23 OF 23 HCAPLUS COPYRIGHT 2005 ACS on STN

AB L-Cystathionine is oxidized by snake venom L-amino acid oxidase at a rate about half that with L-leucine at pH 8.5. The appearance of an absorbance at 296 nm and quantitation of the products of oxidation in the presence of catalase indicate formation in the solns. of a 7-membered ketimine ring produced by cyclization of the monoamino monoketo derivative of cystathionine. A limited double deamination has also been observed In the absence of catalase, S-(carboxymethyl)homocysteine and A-(β-carboxyethyl)cysteine have been identified together with ninhydrin-unreactive compds. yielding the above mentioned carboxy compds. upon hydrolysis with HCl. Authentic samples of the monoamino monoketo analogs of cystathionine have been prepared and compared with the enzymic products. Cyclization of the synthetic products into the ketimine ring is pH-dependent as established by UV spectrum and other assays. Compds. derived from either the oxidation or the reduction of the ketimine have been prepared Many products of enzymic and chemical changes of cystathionine and its ketimine described in the present paper are identical with those identified in the urine of cystathioninuric patients. This result indicates the occurrence in humans of secondary metabolic routes of cystathionine centered on the production of cystathione ketimine, in equilibrium

with the open form, which in cystathioninurics is revealed by the lack of cystathionase.

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FULL ESTIMATED COST                                       102.91     110.42

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)              SINCE FILE      TOTAL
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CA SUBSCRIBER PRICE                                        -7.30      -7.30

FILE 'REGISTRY' ENTERED AT 08:11:51 ON 03 FEB 2005

=> s cyclothionine/cn
L15             1 CYCLOTHIONINE/CN

=> d

L15  ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   105990-93-0  REGISTRY
CN   1,4-Thiazepine-3,5-dicarboxylic acid, hexahydro- (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   Cyclothionine
MF   C7 H11 N O4 S
SR   CA
LC   STN Files:   BIOSIS, CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA  CAplus document type:  Journal; Patent
RL.P   Roles from patents:  BIOL (Biological study); USES (Uses)
RL.NP  Roles from non-patents:  BIOL (Biological study); PROC (Process); RACT
       (Reactant or reagent)
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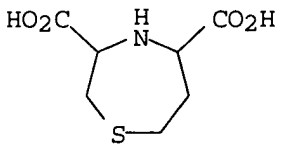


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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

             6 REFERENCES IN FILE CA (1907 TO DATE)
             6 REFERENCES IN FILE CAPLUS (1907 TO DATE)


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COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
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FULL ESTIMATED COST                                         6.87     117.29

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)              SINCE FILE      TOTAL
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CA SUBSCRIBER PRICE                                         0.00      -7.30

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      ESBIOBASE, BIOTECHNO, WPIDS' ENTERED AT 08:12:43 ON 03 FEB 2005
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11 FILES IN THE FILE LIST

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FILE 'LIFESCI'
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FILE 'BIOSIS'
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FILE 'EMBASE'
L21          0 L15

FILE 'HCAPLUS'
L22          6 L15

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L28  ANSWER 1 OF 8  HCAPLUS  COPYRIGHT 2005 ACS on STN
TI   Antagonists of D-amino acid oxidase and D-aspartate oxidase for treatment
     of central nervous sytem disorders
SO   U.S. Pat. Appl. Publ., 138 pp., Cont.-in-part of U.S. Ser. No. 51,681.
     CODEN: USXXCO
IN   Cohen, Daniel; Chumakov, Llya
AN   2003:696521  HCAPLUS
DN   139:224389
     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     --------------      ----   --------    --------------------   --------
PI   US 2003166554        A1    20030904    US 2002-211160         20020801
     US 2003185754        A1    20031002    US 2002-51681          20020116

L28  ANSWER 2 OF 8  HCAPLUS  COPYRIGHT 2005 ACS on STN
TI   Treatment of CNS disorders using D-amino acid oxidase and D-aspartate
     oxidase antagonists
SO   PCT Int. Appl., 194 pp.
     CODEN: PIXXD2
```

IN Cohen, Daniel; Chumakov, Ilya
AN 2002:658287 HCAPLUS
DN 137:195529

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002066672	A2	20020829	WO 2002-IB1262	20020115
WO 2002066672	A3	20040226		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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EP 1412515	A2	20040428	EP 2002-717019	20020115
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JP 2004537275	T2	20041216	JP 2002-566376	20020115

L28 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN
TI Novel Priming Compounds of Cystathionine Metabolites on Superoxide Generation in Human Neutrophils
SO Biochemical and Biophysical Research Communications (2000), 269(2), 297-301
CODEN: BBRCA9; ISSN: 0006-291X
AU Kodama, Hiroyuki; Zhang, Jianying; Sugahara, Kazunori
AN 2000:156231 HCAPLUS
DN 133:3372

L28 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN
TI Characterization of [35S]lanthionine ketimine specific binding to bovine brain membranes
SO Biochemical and Biophysical Research Communications (1993), 195(2), 673-8
CODEN: BBRCA9; ISSN: 0006-291X
AU Dupre, S.; Fontana, M.; Costa, M.; Pecci, L.; Ricci, G.; Cavallini, D.
AN 1993:664740 HCAPLUS
DN 119:264740

L28 ANSWER 5 OF 8 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
DUPLICATE 1
TI PROPERTIES OF THE PHENYLTHIOHYDANTOIN DERIVATIVES OF SOME SULFUR-CONTAINING CYCLIC AMINO ACIDS.
SO Physiological Chemistry and Physics and Medical NMR, (1988) Vol. 20, No. 3, pp. 199-204.
CODEN: PCPNER. ISSN: 0748-6642.
AU PECCI L [Reprint author]; COSTA M; PINNEN F; ANTONUCCI A; CAVALLINI D
AN 1989:199153 BIOSIS

L28 ANSWER 6 OF 8 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
DUPLICATE 2
TI HEXAHYDRO-1 4-THIAZEPINE-3 5-DICARBOXYLIC ACID AND THIOMORPHOLINE-3 5-DICARBOXYLIC ACID ARE PRESENT IN NORMAL HUMAN URINE.
SO Proceedings of the National Academy of Sciences of the United States of America, (1987) Vol. 84, No. 15, pp. 5111-5114.
CODEN: PNASA6. ISSN: 0027-8424.
AU MATARESE R M [Reprint author]; PECCI L; RICCI G; NARDINI M; ANTONUCCI A; CAVALLINI D
AN 1987:427426 BIOSIS

L28 ANSWER 7 OF 8 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN

TI THE OXIDATION OF CYCLOTHIONINE BY D ASPARTATE OXIDASE.
SO Physiological Chemistry and Physics and Medical NMR, (1986) Vol. 18, No. 1, pp. 71-74.
CODEN: PCPNER. ISSN: 0748-6642.
AU SOLINAS S P [Reprint author]; SANTORO L; ANTONUCCI A; CAVALLINI D
AN 1987:9803 BIOSIS

L28 ANSWER 8 OF 8 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
TI GAS-CHROMATOGRAPHIC MASS-SPECTROMETRIC DETECTION OF 1 4 HEXAHYDROTHIAZEPINE-3 5-DICARBOXYLIC-ACID CYCLOTHIONINE IN BOVINE BRAIN.
SO Journal of Biological Chemistry, (1985) Vol. 260, No. 29, pp. 15577-15579.
CODEN: JBCHA3. ISSN: 0021-9258.
AU CAVALLINI D [Reprint author]; PECCI L; MATARESE R M; RICCI G; ACHILLI M
AN 1986:144901 BIOSIS

=> d ab 1-
YOU HAVE REQUESTED DATA FROM 8 ANSWERS - CONTINUE? Y/(N):y

L28 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN
AB Compds. that are antagonists of D-amino acid oxidase and D-aspartate oxidase, methods of treating CNS disorders including bipolar disorder, psychosis and schizophrenia using the compds., and pharmaceutically acceptable compns. that contain the antagonists are disclosed. The enzymes were identified as candidate drug targets when two-hybrid screening showed that the enzymes interact with the g34872 protein associated with schizophrenia and bipolar disorder. Anal. of the activation of swine kidney D-amino acid oxidase by g34872 is presented.

L28 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN
AB Compds. that are antagonists of D-amino acid oxidase and D-aspartate oxidase, methods of treating CNS disorders including bipolar disorder, psychosis and schizophrenia using the compds., and pharmaceutically acceptable compns. that contain the antagonists are disclosed.

L28 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN
AB Human peripheral blood polymorphonuclear leukocytes were preincubated with cystathionine and cystathionine metabolites found in the urine of patients with cystathioninuria. Among the cystathionine metabolites, cystathionine ketimine and N-acetyl-S-(3-oxo-3-carboxy-n-propyl) cysteine (NAc-OCPC) significantly enhanced the N-formylmethionylleucylphenylalanine (fMLP)-induced superoxide generation, but cystathionine, NAc-cystathionine, and cyclothionine did not enhance the superoxide generation. Cystathionine ketimine and NAc-OCPC also enhanced superoxide generation induced by opsonized zymosan (OZ) but not that induced by arachidonic acid (AA) and phorbol 12-myristate 13-acetate (PMA). Superoxide generation induced by cystathionine ketimine and NAc-OCPC was inhibited by genistein, an inhibitor of tyrosine kinase, and was enhanced by 1-(5-isoquinoline sulfonyl)-2-methylpiperazine (H-7), an inhibitor of protein kinase C. Cystathionine ketimine and NAc-OCPC markedly also increased phosphorylation of 45-kDa protein in human neutrophils and the phosphorylation depended on the concns. of cystathionine ketimine and NAc-OCPC. The phosphorylation of 45-kDa protein induced by cystathionine ketimine and NAc-OCPC was inhibited by genistein and herbimycin A, inhibitors of tyrosine kinase, but was not inhibited by H-7 and staurosporine, inhibitors of protein kinase C. Cystathionine metabolites and L-cystathionine sulfoxides were separated into two diastereoisomers, CS-I and CS-II. CS-I enhanced the superoxide generation induced by AA and PMA but not that induced by fMLP and OZ. In contrast, CS-II enhanced the superoxide generation induced by fMLP and OZ, but not that induced by AA and PMA. (c) 2000 Academic Press.

L28 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN
AB [35S]Lanthionine ketimine binds specifically and with high affinity to

bovine brain membranes. This binding has been studied in detail. It is reversible, not occurring at an uptake site or at a metabolizing enzyme and depending only weakly on ionic strength; it is affected by thiol reagents. [35S]Lanthionine ketimine specific binding is displaced only by other ketimines and by catecholamines, but not by more selective adrenergic ligands; binding parameters are reported. [3H]Adrenaline but not [3H]dihydroalprenolol is partially displaced by lanthionine ketimine. With bovine brain prepns. a significant stimulation of basal adenylate cyclase activity by lanthionine ketimine is observed

L28 ANSWER 5 OF 8 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
DUPLICATE 1
AB 1,4-thiomorpholine-3-carboxylic acid (TMA), hexahydro-1,4-thiazepine-3,5-dicarboxylic acid (cyclothionine) and their respective unsaturated analogues lanthionine ketimine (LK) and cystathionine ketimine (CK) react with phenylisothiocyanate to give the phenylthiohydantoin (PTH) derivatives without acidification and heating steps. Moreover the PTH-derivatives of the ketimines show a characteristic absorption maximum at 380 nm. Treatment with 1 M ammonia at 100° C converts the PTH-TMA in the corresponding PTH-ketimine. These properties are peculiar of these cyclic sulfur compounds.

L28 ANSWER 6 OF 8 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
DUPLICATE 2
AB Hexahydro-1,4-thiazepine-3,5-dicarboxylic acid and thiomorpholine-3,5-dicarboxylic acid, simply referred to as cyclothionine and TMDA, respectively, are two cyclic sulfur-containing imino acids detected in bovine brain. Human urine has been investigated to establish the occurrence of these imino acids as common constituents under normal conditions. The morning urine of healthy subjects has been analyzed for enrichment of these compounds by using an ion-exchange procedure. Gas/liquid chromatography of the final extracts revealed the presence of peaks coeluting with authentic cyclothionine and TMDA. The latter compound eluted very close to an unknown sulfur-containing compound. A resolved peak of TMDA has been obtained by high-performance liquid chromatography of the final extracts derivatized with phenylisothiocyanate. Selected ion monitoring with multiple-ion detection applied to the compounds separated by gas chromatography revealed the presence of the respective molecular ions and of the decarboxylated fragments, thus confirming the identification of cyclothionine and TMDA in human urine.

L28 ANSWER 7 OF 8 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
AB Cyclothionine was found to be a subtrate for bovine kidney D-Aspartate oxidase. The substrate, prepared chemically as a mixture of the possible stereoisomers, exhibits an inhibition at elevated concentrations. Compounds structurally related to cyclothionine, like TMDA and α-α'-iminodipropionic acid, have also been assayed with the enzyme.

L28 ANSWER 8 OF 8 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
AB Cystathionine has been reported to undergo enzymatic changes leading to the formation of seven membered cyclic products (Ricci, G., Santoro, L., Achilli, M., Matarese, R. M., Nardini, M., and Cavallini, D. (1983) J. Biol. Chemical 258, 10511-10517; Cavallini, D., Costa, M., Pensa, B., and Coccia, R. (1985) Biochem. Int. 10, 641-646). Gas-chromatographic and mass-spectrometric evidence reported in this paper indicates that the cyclic derivative of cystathionine, 1,4-hexahydrothiazepine-3,5-dicarboxylic acid, here simply named cyclothionine, is a normal component of bovine brain. This finding together with the detection of the same compound in the urine of cystathioninuric patients (Kodama, H., Sasaki, K., Mikasa, H., Cavallini, D., and Ricci, G. (1984) J. Chromatogr. 311, 183-188) supports the conclusion that cystathionine, apart from its role in trans-sulfuration, is converted also into cyclic compounds whose

biochemical significance is as yet unknown.

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FULL ESTIMATED COST                              53.31     170.60

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)    SINCE FILE      TOTAL
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CA SUBSCRIBER PRICE                              -2.92     -10.22

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